ENDOCRINOLOGÍA Y NUTRICIÓN

An unexplained cause of superior vena cava syndrome

A 65-year-old female patient with a history of high blood pressure, type 2 diabetes mellitus, atrial fibrillation, morbid obesity, and obstructive sleep apnea syndrome attended the emergency room suffering from hypotension, upper limb edema, and dyspnea. NIMV could not, therefore, be completely withdrawn. A transthoracic echocardiogram showed a left ventricle with a preserved size, shape, and contractility (ejection fraction, 65%) and no valve changes. Based on these results, intravenous albumin was added to treatment. While a negative balance was achieved and lower limb edema decreased, tachypnea, orthopnea, and asymmetric edema in the upper limbs and right breast persisted. Collateral chest circulation andjugular engorgement were also found.

A computed tomography (CT) scan of the neck and chest revealed the presence of a hypervascularized bulky mass of heterogeneous density and with relatively well-delimited margins, 10 x 8.5 x 13 cm in size, occupying the upper and anterior mediastinum and compressing adjacent structures (trachea, supra-aortic trunks, venous brachiocephalic trunk, and aortic arch) (Fig. 1). SVC size was decreased, and prominent collateral circulation was seen in the distal cervical region and anterior chest wall, which was probably related to chronic impairment in venous return.

The mass also showed loss of the fat plane of separation from the left thyroid lobe, thus suggesting a thyroidal origin as a first possibility. Bilateral pleural effusion was also found.

Thyroid hormone measurements found the following levels: thyrotropin (TSH), <0.015 µIU/mL (reference range [RR], 0.465-4.68); unbound thyroxine (free T4), 6.35 ng/dL (RR, 0.78-2.19); unbound triiodothyronine (free T3), 6.61 pg/mL (RR, 2.77-5.27). Antithyroid antibody levels were not measured. Ultrasound-guided fine needle aspiration of the thyroid gland was performed. The pathological laboratory reported the presence of thyroid hyperplasia.

Based on these results, confirming the presumed diagnosis of SVCS, a vascular stent was placed in the right brachiocephalic trunk, but no respiratory improvement was achieved. Definitive surgical treatment, consisting of total thyroidectomy, was therefore decided upon.

The pathological laboratory reported a surgical specimen 384 g in weight and 12 x 9 x 6 cm in size. Microscopic description confirmed the presence of thyroid nodular hyperplasia, predominantly macrofollicular, with no evidence of malignancy. These results supported the diagnosis of SVCS secondary to intrathoracic goiter.

Superior vena cava syndrome (SVCS) is an uncommon condition characterized by a series of signs and symptoms derived from total or partial obstruction of blood flow through the superior vena cava (SVC) to the right atrium. This results in a decreased venous return to the head, neck, and upper limbs. More than 90% of cases of SVCS are caused by malignant tumors, among which lung carcinoma is the most common. Other responsible tumors include non-Hodgkin lymphoma and metastatic tumors. Benign causes of SVCS may include mediastinal fibrosis, thrombosis, syphilitic aneurysm, and tuberculous mediastinitis. Iatrogenic SVCS has occurred increasingly in recent years due to the increased use of intravenous central catheters for purposes such as the administration of chemotherapy or parenteral nutrition. Intrathoracic goiter is a very uncommon cause of SVCS.

A case of SVCS secondary to intrathoracic goiter is reported below.

A 65-year-old female patient with a history of high blood pressure, type 2 diabetes mellitus, atrial fibrillation, morbid obesity, and obstructive sleep apnea syndrome attended the emergency room suffering from a four-day progressive dyspnea accompanied by an increased loss of consciousness. The findings of the physical examination included a mean blood pressure of 60 mmHg, in addition to anasarca. Cardiopulmonary examination revealed arrhythmic, low intensity heart sounds, decreased vesicular murmur in both lung bases, and severe bronchospasm. Chest X-rays showed an enlarged upper mediastinum and signs consistent with acute pulmonary edema. During examination, the patient experienced respiratory arrest requiring the start of cardiopulmonary resuscitation maneuvers, after which the patient recovered an irregular respiratory rate for which noninvasive mechanical ventilation (NIMV) was needed.

Treatment was started with intravenous furosemide and dopamine as a continuous infusion, after which the patient experienced a slight clinical improvement, but continued suffering from hypotension, upper limb edema, and dyspnea. NIMV could not, therefore, be completely withdrawn.

A transthoracic echocardiogram showed a left ventricle with a preserved size, shape, and contractility (ejection fraction, 65%) and no valve changes. Based on these results, intravenous albumin was added to treatment. While a negative balance was achieved and lower limb edema decreased, tachypnea, orthopnea, and asymmetric edema in the upper limbs and right breast persisted. Collateral chest circulation and jugular engorgement were also found.

A computed tomography (CT) scan of the neck and chest revealed the presence of a hypervascularized bulky mass of heterogeneous density and with relatively well-delimited margins, 10 x 8.5 x 13 cm in size, occupying the upper and anterior mediastinum and compressing adjacent structures (trachea, supra-aortic trunks, venous brachiocephalic trunk, and aortic arch) (Fig. 1). SVC size was decreased, and prominent collateral circulation was seen in the distal cervical region and anterior chest wall, which was probably related to chronic impairment in venous return.

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The pathological laboratory reported a surgical specimen 384 g in weight and 12 x 9 x 6 cm in size. Microscopic description confirmed the presence of thyroid nodular hyperplasia, predominantly macrofollicular, with no evidence of malignancy. These results supported the diagnosis of SVCS secondary to intrathoracic goiter.
Following surgery, the patient experienced severe respiratory difficulty secondary to pulmonary atelectasis and eventually died.

SVCS was described by William Hunter in 1757, and the first clinical case of SVCS secondary to benign intrathoracic goiter was reported by McArt in 1954. Patients with SVCS usually experience dyspnea and facial plethora, to which dysphagia, headache, lethargy, and syncope may be associated. Coma secondary to cerebral edema and stridor due to laryngeal edema are markers of extreme severity. In SVCS secondary to thyroid disease, initial clinical signs are usually insidious, unless triggering factors such as intratumoral hemorrhage exist. These symptoms may be aggravated in the supine position, which suggests significant changes in airway lumen. Characteristic clinical findings include vein dilatation in the neck, an increased number of collateral veins in the anterior chest wall, cyanosis, and edema of the face, arms, and chest, all of them symptoms seen in our patient. Respiratory or cardiac arrest may occur, especially in patients receiving sedatives or under general anesthesia.

Diagnosis of SVCS is essentially based on clinical signs and symptoms. Several imaging techniques may also be used, of which chest X-rays are the most important. The most significant finding in chest X-rays is the widening of the upper mediastinum. A lower proportion of patients also have pleural effusion (as seen in the X-ray film of the reported patient). CT scans provide a better visualization of mediastinal anatomy, adequately define the level and extent of venous return blockade, identify collateral circulation pathways, and show the cause of SVCS with 92% sensitivity and 96% specificity. Magnetic resonance imaging has no advantages over CT in terms of diagnosis, but is a diagnostic option in patients allergic to iodinated contrasts or in whom venous access is not possible.

Treatment of SVCS depends on its cause. Symptoms condition adequate initial management of this pathology. Thus, SVCS secondary to a tumor requires radiotherapy or chemotherapy as part of the treatment. Placement of intravascular stents is another palliative option for medical intervention while waiting for definitive treatment. Stent placement allows for hemodynamic improvement of venous compression, and is therefore a therapeutic option in patients with severe symptoms such as respiratory distress, stridor, or decreased consciousness. This option may also be considered for cancer patients not responding to chemotherapy or radiotherapy, and is of particular value in cases of SVCS secondary to thrombosis. Complications of this procedure, including severe hemorrhage, pulmonary embolism, insertion site hematoma, stent migration and, very rarely, perforation have been reported in 3%-7% of patients with SVCS.

As regards definitive treatment, surgery is seldom considered because of its high morbidity and mortality rate and limited life expectancy, particularly in patients with SVCS secondary to neoplasm. Intrathoracic goiter causing SVCS is one of the few conditions for which surgery is indicated. SVCS prognosis is related to its cause, and the mortality rate during surgery for intrathoracic goiter ranges from 3%-4%.

In the reported patient, a stent was implanted while waiting for the surgical team’s decision as to the definitive treatment to be followed. Thyroidectomy was finally decided upon, despite the high surgical risk attached. Unfortunately, the therapeutic outcome was not the one hoped for.

References
DiGeorge syndrome with mild episodic hypocalcemia
Síndrome de DiGeorge con hipocalcemia transitoria leve

DiGeorge syndrome occurs in one out of every 4,000 to 9,700 live births\(^1\). The genetic defect responsible has been found to be deletion in the 22q11.2 region, and the condition is thus currently included in the group of disorders of the 22q11 deletion syndrome. Cardiac malformations, immunodeficiency, hypocalcemia, palate malformations with velopharyngeal insufficiency, learning difficulties, and arrested development have mainly been reported. Genitourinary malformations, psychiatric disease, and bone and joint changes are less commonly found\(^3\). CATCH 22 (Cardiac defects, Abnormal facial features, Thymic hypoplasia, Cleft palate and Hypocalcemia) is the acronym used for these conditions.

We report the case of a 30-year-old female patient referred to the endocrinology outpatient clinic for low weight. Her personal history included surgery for patent ductus arteriosus at age 5 months, tremor with atypical myoclonic features, gothic palate, fracture of both kneecaps, lumbar scoliosis, hyperkyphosis and hyperlordosis, chondromalacia patella, rheumatic fibromyalgia, biphasic Raynaud's phenomenon, anemia and mild fluctuating thombocytopenia, endometriosis, and adenoidectomy. She had no toxic habits and worked in a company for disabled people. Her family history included cases of malignant tumors, but no early deafness or blindness, nor known hereditary diseases. On direct questioning, the patient reported no rapid weight loss, recent changes in food intake, or incorrect feeding habits. She had previously stopped swimming because of weakness. There were no gastrointestinal symptoms, nor thyroid or adrenal symptoms. The patient denied excessive thirst. The physical examination showed: weight, 43.5 kg; height, 163 cm; BMI, 16 kg/m\(^2\). It also revealed the following: decreased muscle mass with preserved force; supine and sitting blood pressure values of 100/60 mmHg and 105/60 mmHg respectively; rhythmic pulse at 84 bpm; elongated face with microstomy; no oculomotor nerve paresis; no goiter palpated; no skin hyperpigmentation; normal cardiopulmonary auscultation; no abdominal masses palpated; no edema. Endocrinological work-up revealed normal results with regard to thyroid function, pituitary-adrenal axis, carbohydrate metabolism, and urinary catecholamine and metanephrine levels, with normal kidney and liver function. Laboratory tests showed no changes in standard nutritional parameters and trace elements. However, hypocalcemia (8.0 mg/dL, normal range, 8.6-10.2) with no associated hypoalbuminemia, normal phosphorus and decreased calcidiol levels (15 mcg/L, normal range 19-57) with no compensatory increase in parathormone levels (28 ng/L, normal levels 12-72) were found. Magnesium levels measured at the same time were also normal. Total 24-hour urine output was less than 1,000 mL on several occasions, and the calcium/creatinine ratio was estimated in fresh urine. In previous laboratory tests, calcium levels were almost always within the normal range, along with normal parathormone (Table 1), protein, and albumin levels. A review of the pediatric history confirmed recurrent pneumonitis since 15 months of age. A positive Mantoux test, positive cultures for *Giardia lamblia*, and common childhood viral infections were also found. Presumptive diagnoses were low weight with no proven endocrine etiology, mild vitamin D deficiency, and possible CATCH-22 syndrome. Adequate weight gain was achieved through customized dietary treatment. The genetics department confirmed the clinical suspicion and issued a diagnosis of 22q11.2 deletion syndrome. Abdominal ultrasound showed no urinary tract malformations. At the next visit, the patient had normal calcium levels without oral calcium or vitamin D supplementation and no changes in symptoms. Immunocompetence was assessed by the hematology department. We scheduled laboratory follow-up of phosphorus and calcium metabolism to start treatment based on calcium, phosphorus, calcidiol, and calcitriol levels and bone mineral density.

The patient was diagnosed at an uncommon age. Patients with DiGeorge syndrome are usually diagnosed in childhood based on the presence of congenital heart disease,